Circulating PCSK9 levels are not associated with the severity of hepatic steatosis and NASH in a high-risk population

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Résumé en anglais	Background and aims Some studies suggested that proprotein convertase subtilisin kexin type 9 (PCSK9) is linked to liver steatosis severity and non-alcoholic steatohepatitis (NASH). We aimed to assess whether circulating PCSK9 levels are associated with either liver fat content (LFC) or histological markers of NASH in high-risk patients. Methods We present results from three cross-sectional studies from two French Hospitals: Dijon and Numevox (departments of Endocrinology) and Angers (department of Hepatology). Only patients without lipid-lowering therapy were included. All 132 patients had type 2 diabetes in Dijon, compared to 55/224 in Numevox (25%) and 39/122 in Angers (32%). LFC was assessed on MRI (Dijon and Numevox), and NASH lesion on liver biopsy (Angers). Additionally, we included mRNA results from 138 overweight patients of a Belgian Hospital (Antwerp). Results While circulating levels of PCSK9 were positively correlated with total cholesterol, LDL-C, triglycerides and non-HDL-C in all 3 cohorts, no significant association was found between PCSK9 and transaminases. Furthermore, no association was found between plasma PCSK9 levels and LFC in both Numevox (βadjusted = 0.71 ± 1.33, p = 0.60) and Dijon (βadjusted = −1.03 ± 0.90, p = 0.25). There was no correlation between circulating PCSK9 and histological liver lesions: steatosis severity (βadjusted = −3.95 ± 2.75, p = 0.15), NASH activity score (βadjusted = −0.31 ± 0.17, p = 0.082), lobular (β = −0.067 ± 0.055, p = 0.22) or portal inflammation (β = −0.088 ± 0.079, p = 0.27), ballooning (β = −0.025 ± 0.065, p = 0.70) and fibrosis (β = −0.17 ± 0.11, p = 0.12). Finally, hepatic PCSK9 mRNA levels were not correlated with NASH histological severity. Conclusions Circulating PCSK9 concentrations are not associated with the severity of liver steatosis or histological markers of NASH. These data are reassuring regarding the clinical use of PCSK9 inhibitors in cardiovascular diseases.
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